

FIG. 1

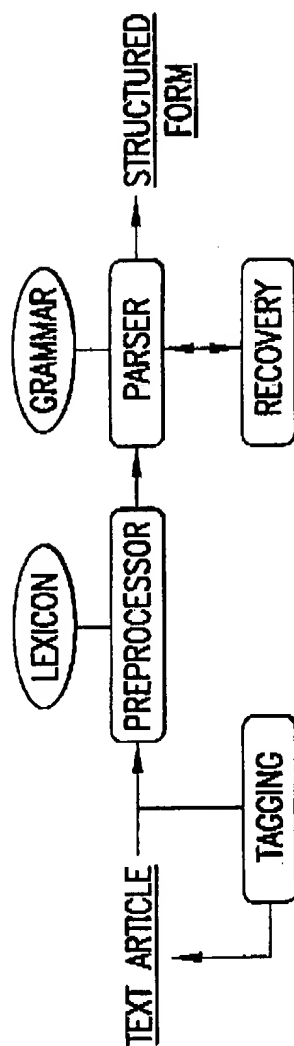
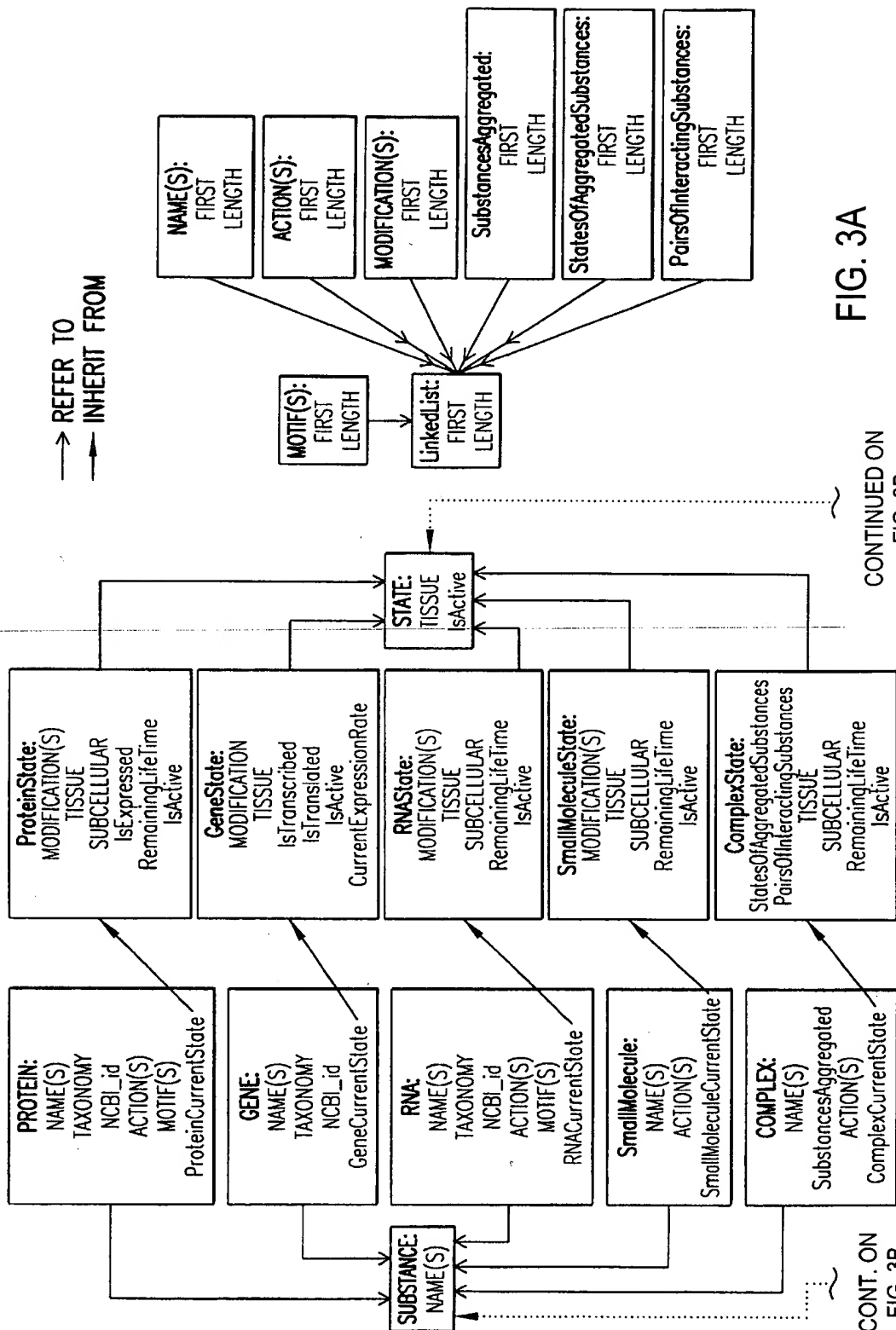
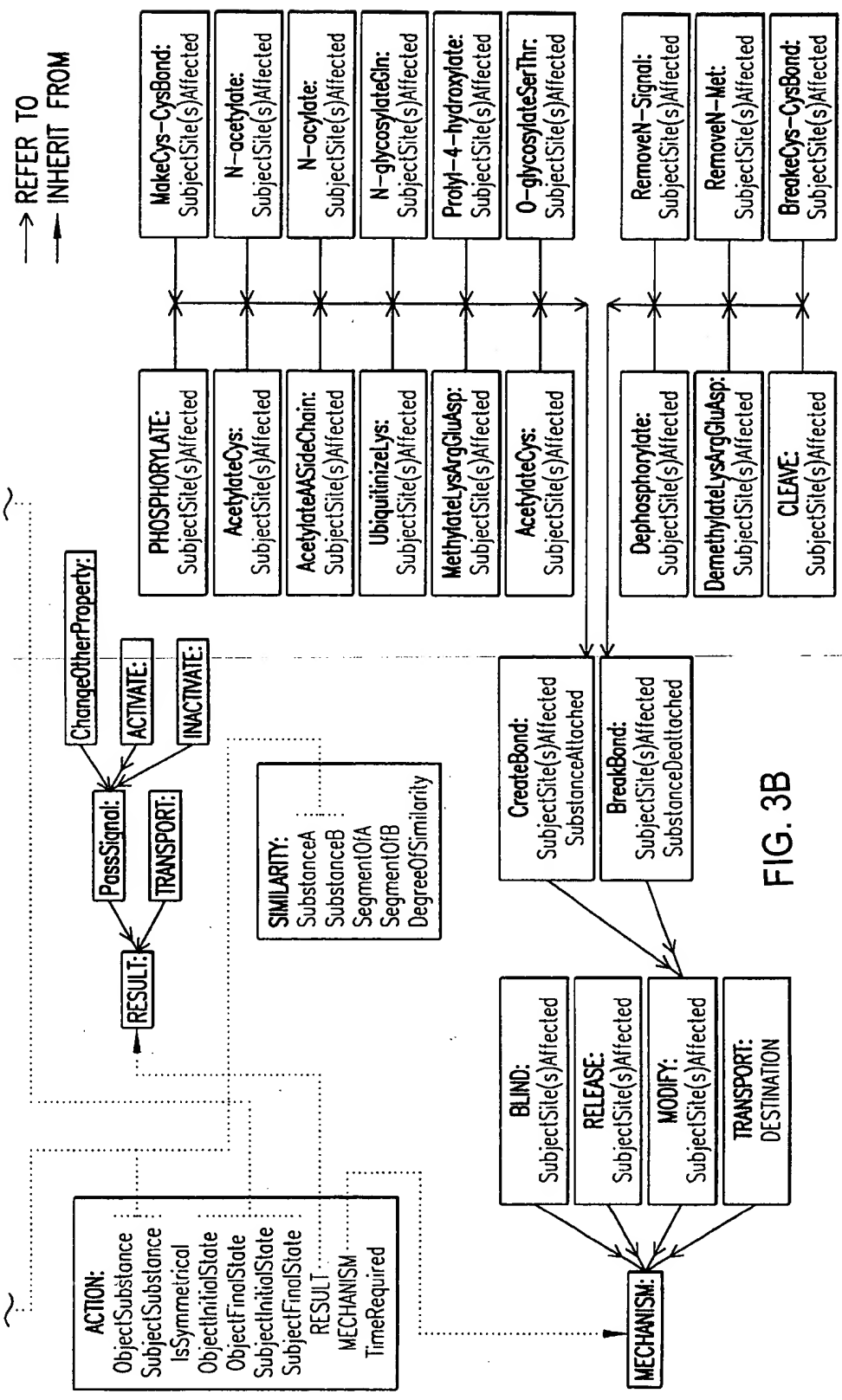


FIG. 2



CONT. FROM
FIG. 3A

CONTINUED FROM
FIG. 3A





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bcl-xL / bcl / bcl-xS / ced-9 / Bax / Bcl / Bcl / p21 / NGF1-B / N10 / Nk1 / Nur77 / Nur1 / Nor-1 / Noi-1 / RXR / galectin-1 / N-glycan / CNTF / lck / fyn / ZAP-70 / raf / ras / MAP / protein kinase C / PKC / phosphatase calcineurin / NF-AT / AP1 / 14-3-3 / Raf-1 / Bcl-2 / interleukin / IL-1 / IL-3 / cytokine / IGF-1 / CD95 / Apo-1 / RIP / FAF1 / FADD / FAP-1 / TNFR / TRAF / TRAP1 / TRAP2 / TRADD / H1AP1 / H1AP2 / CD40 / CD30 / XIAP / CD2 / CD3 / TCR / Bcl-w / Mcl-1 / NR-13 / BHRF1 / HMW5-HL / E1B19K / Nbk / Mch2 / CPP32 / ICE / FLICE / Nedd-2 / TX / Mch3 / Mch4 / ICB-1s / nor-1 / DNaseI / caspase / MACH1 / Mch5 / apopain / Yama / ICH / CMH / ced-3 / ced-4 / ced-9 / p53 / MKK1 / MKK2 / MKK4 / BAG-1 / Src / FAST / p38 / p42 / ERK1 / p44 / ERK2 / SAPK / JNK / MEK / C-JUN / MEF2D / ATF2 / calcineurin / ELK-1 / protein phosphatase 2A / raf-1 / IL-1 beta / TNF / PTK / Apaf / p35 / ETS / C-Myc / IL-2 / IL-2 receptor / NF-kappa B / TNFR-1 / TRAIL / APO-2L / DR4 / death receptor / DR3 / DR2 / DR5 / DR1 / bod / BMPR / BMP-x / TGF / grim / bid / FAN / perforin / Fas-L / Fas / DcR1 / decoy receptor / wxi-1 / NGF receptor / growth factor / RAR

FIG. 4

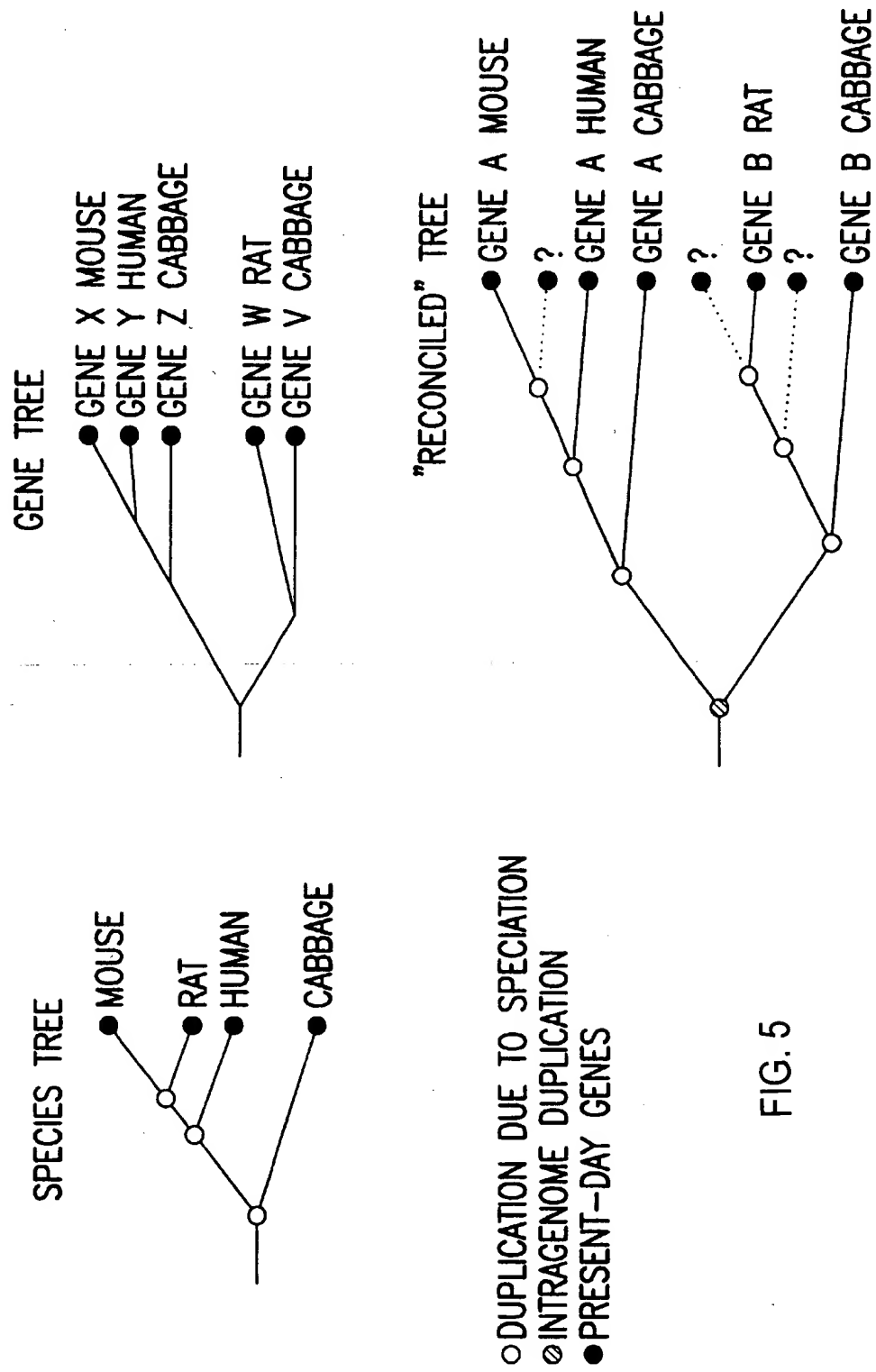
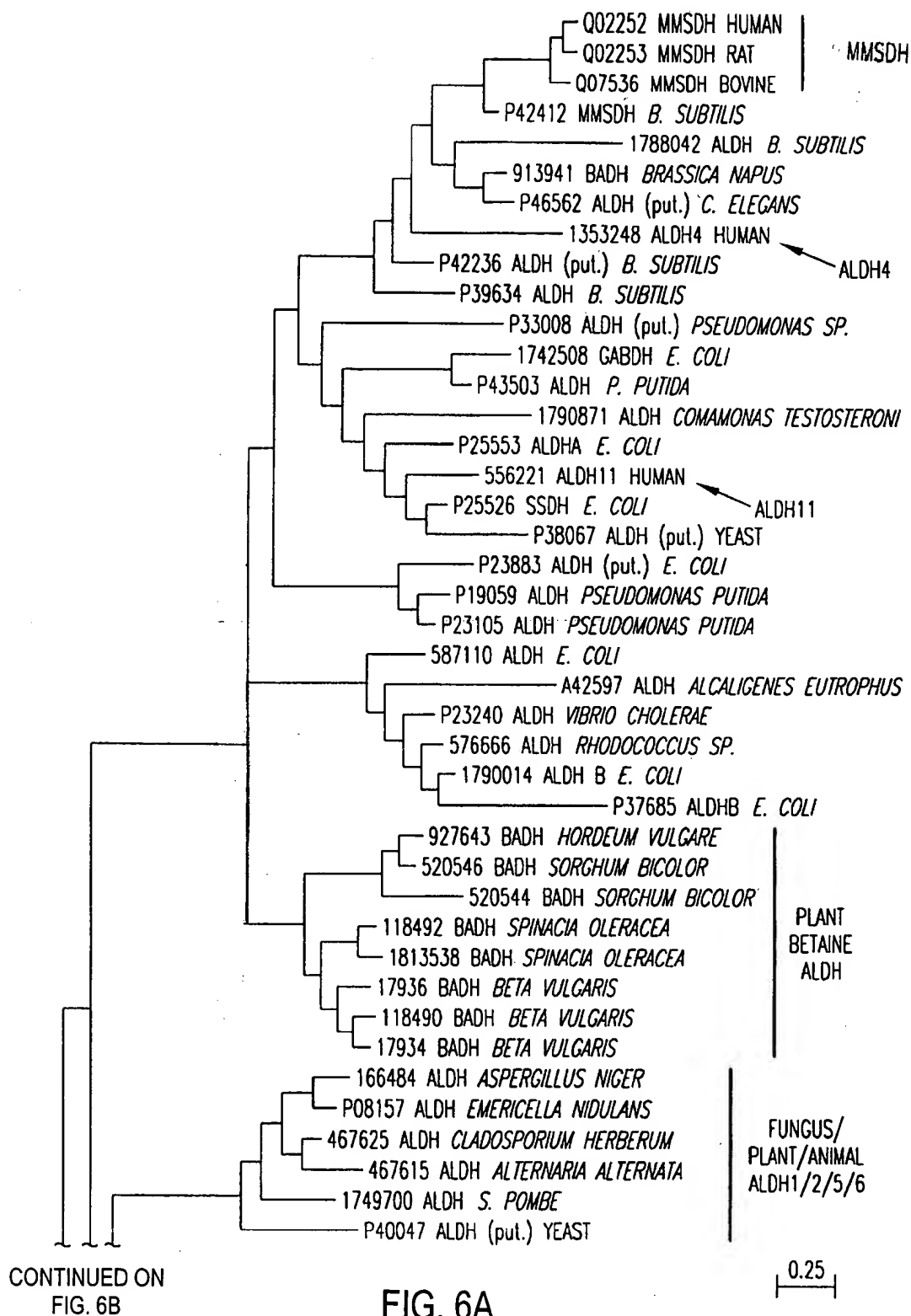


FIG. 5

○ DUPLICATION DUE TO SPECIATION
 ⊗ INTRAGENOME DUPLICATION
 ● PRESENT-DAY GENES



CONTINUED FROM
FIG. 6A

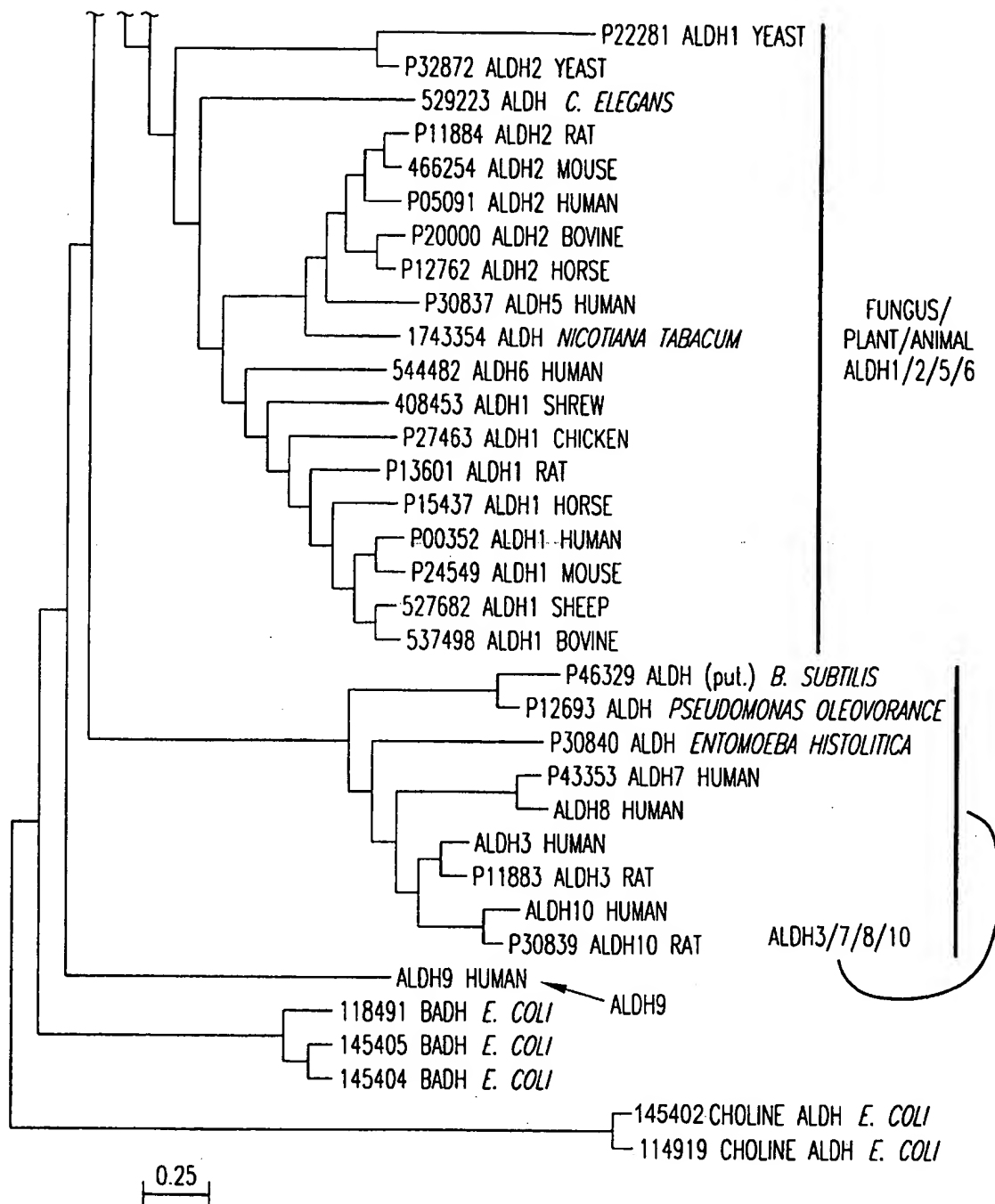
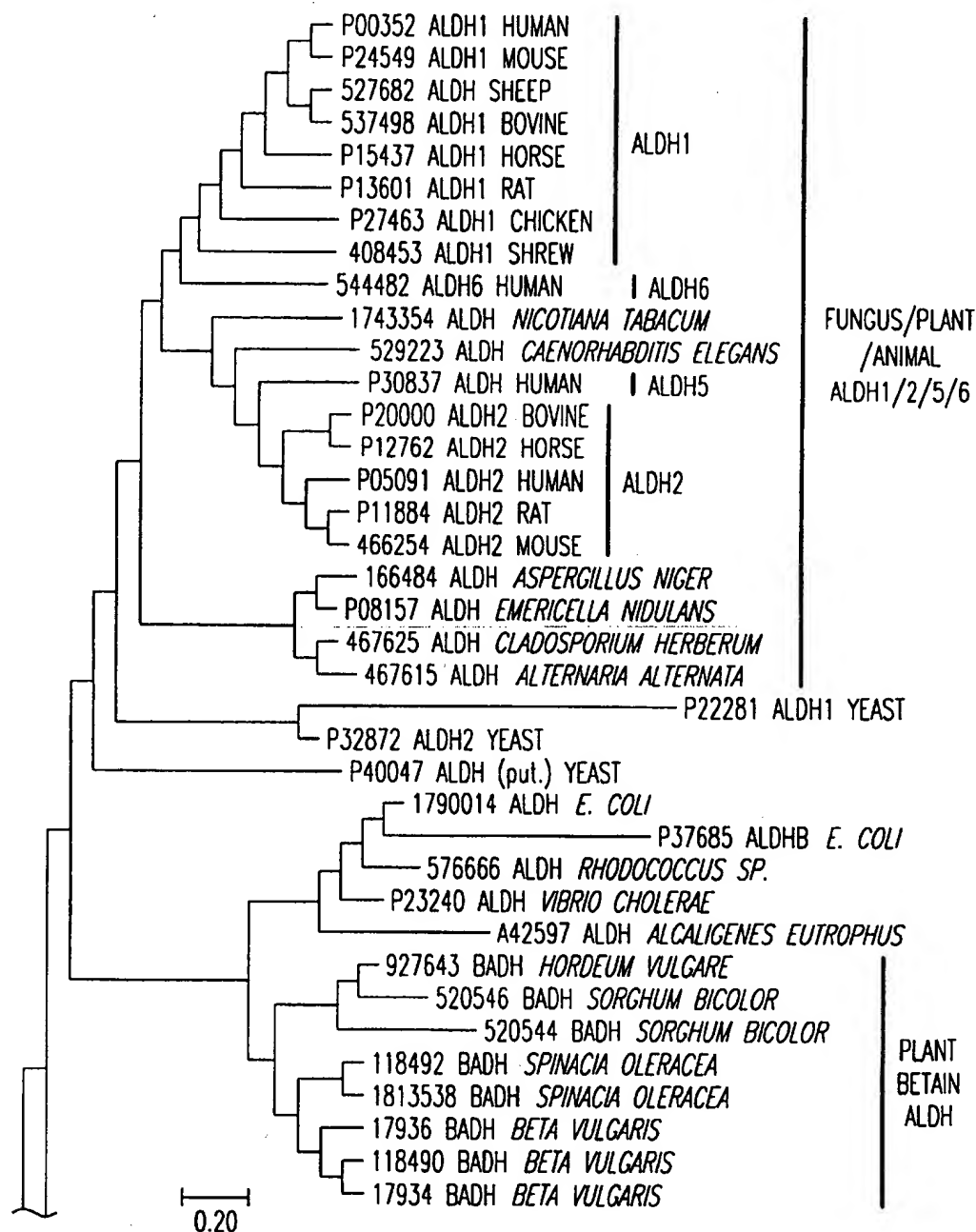


FIG. 6B



CONTINUED ON
 FIG. 7B

FIG. 7A

CONTINUED FROM
FIG. 7A

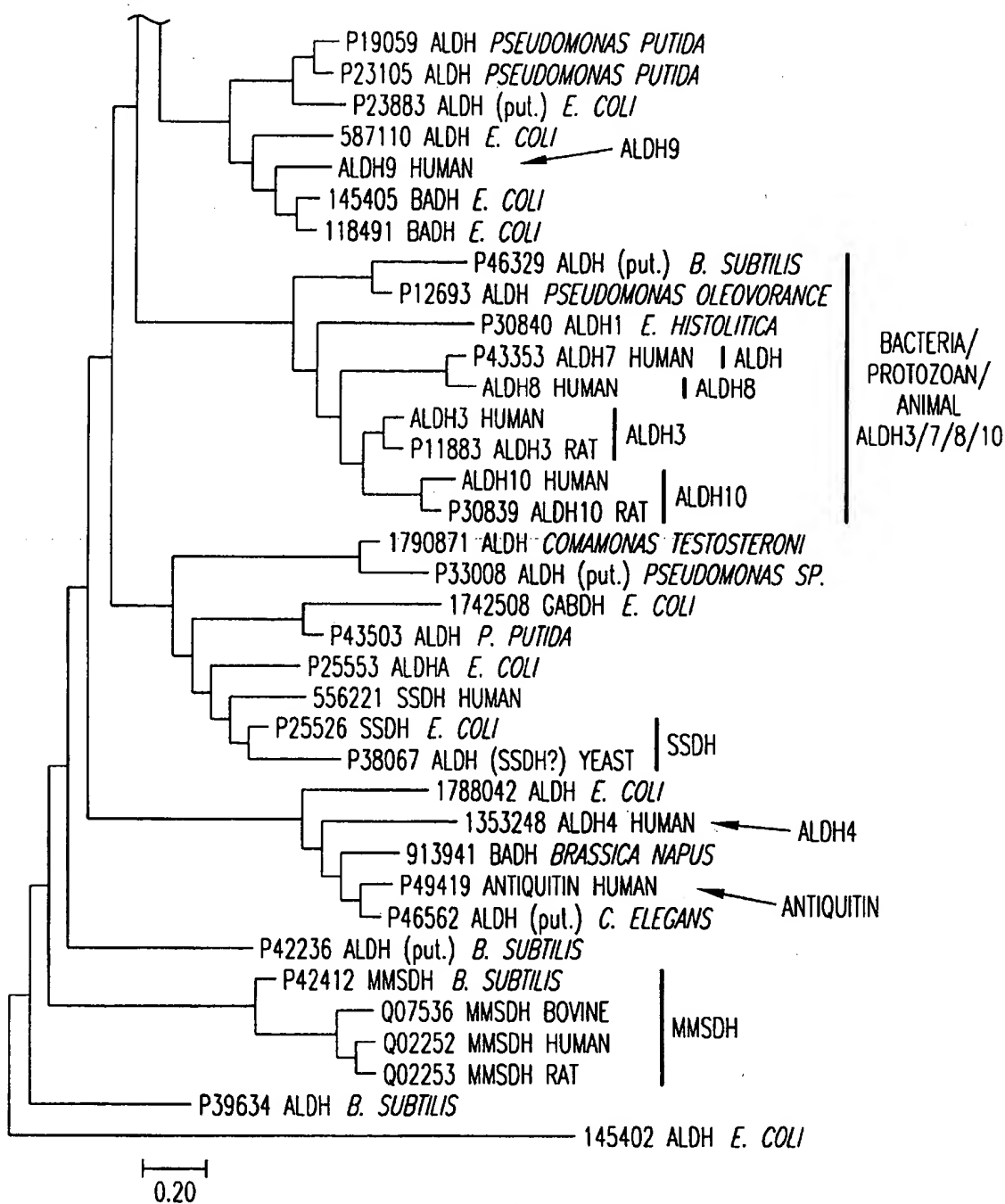
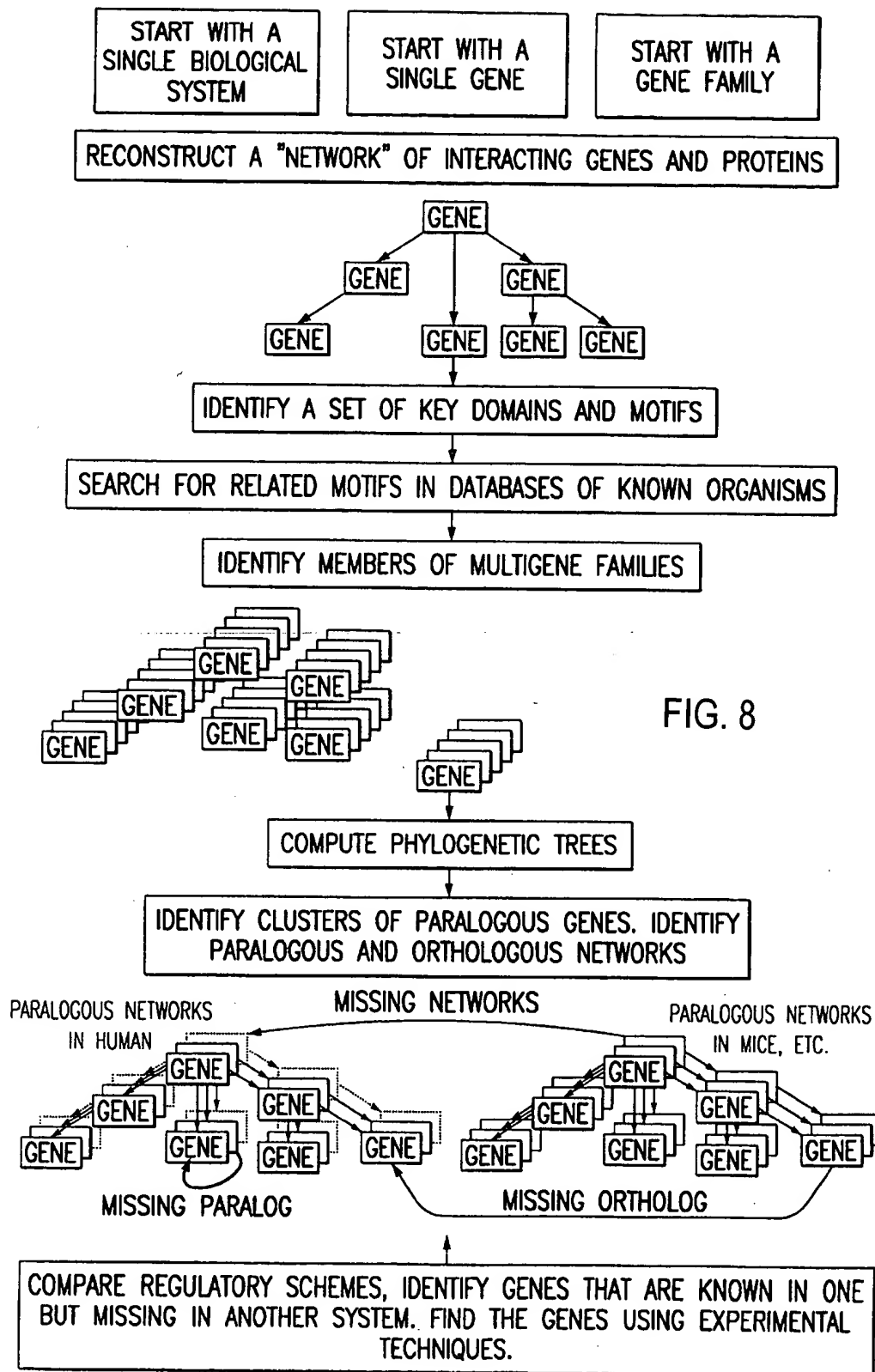
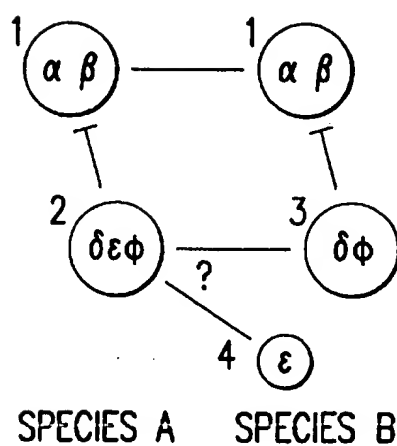
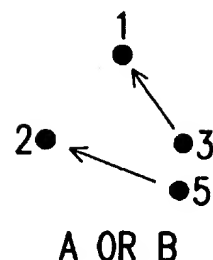
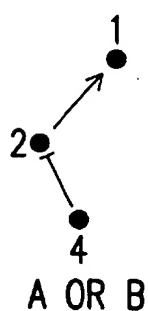
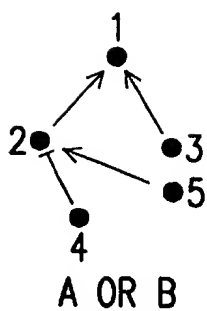
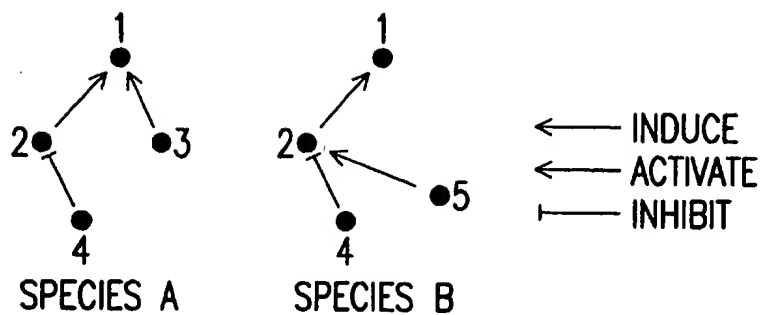


FIG. 7B







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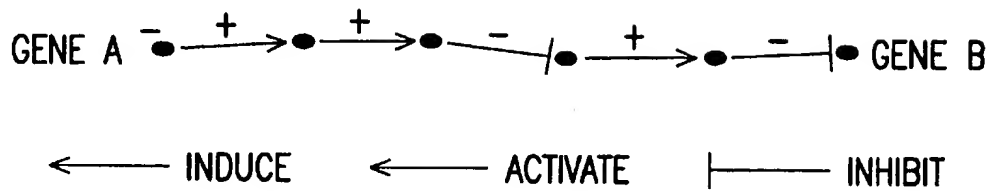


FIG. 11A

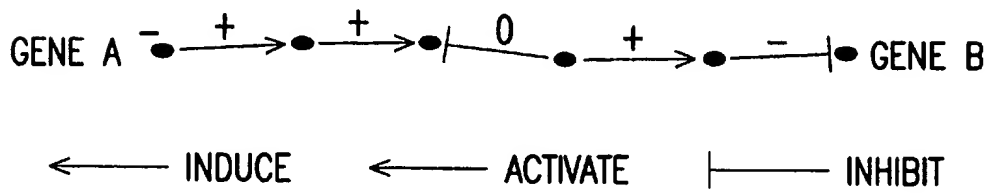


FIG. 11B

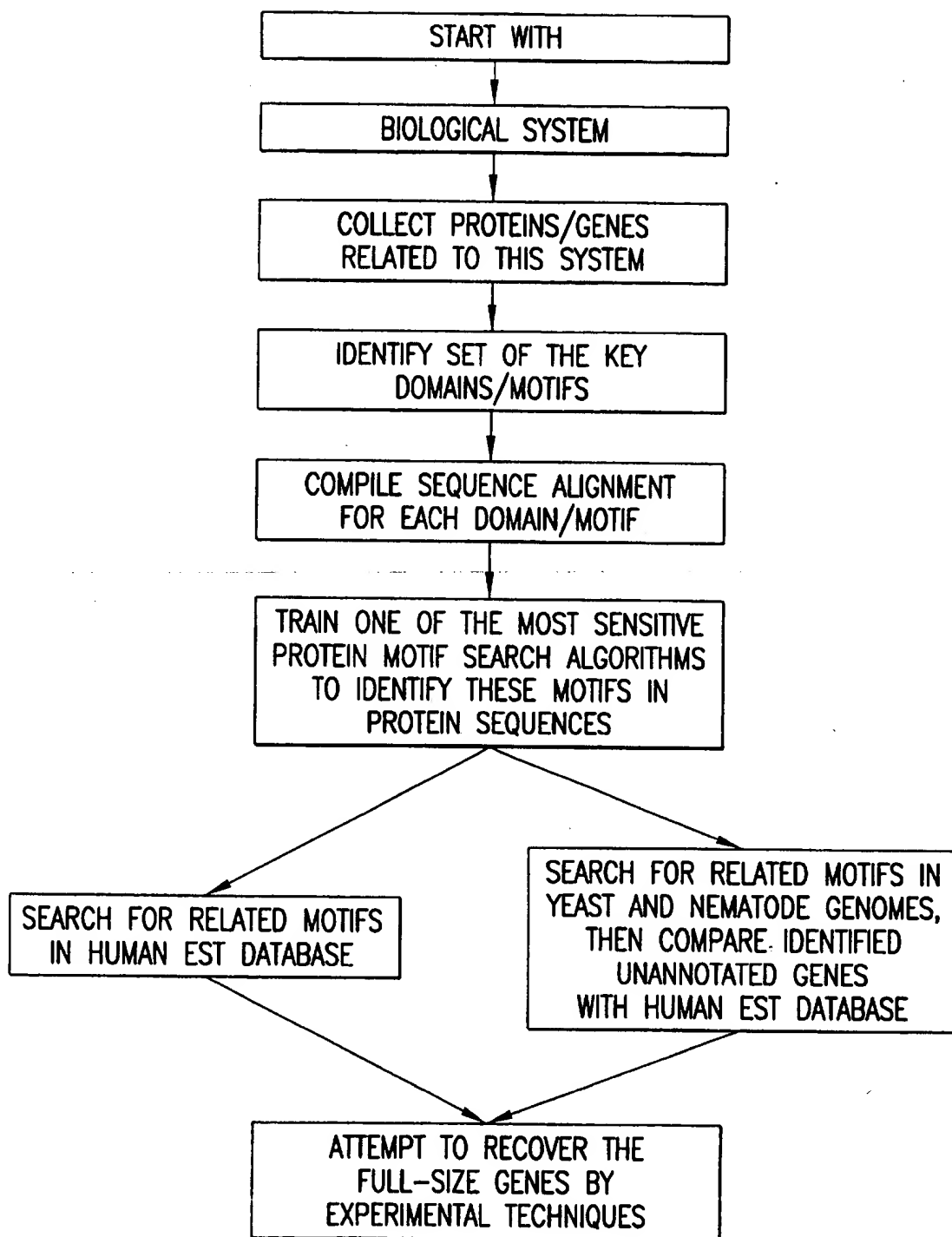


FIG. 12

LEGEND FOR FIGS. 13A, 13B AND 13C

☆	POZ/BTB DOMAIN	⤴	TRANSMEMBRANE HELIX	⬭	NEW (?) TN (TUMOR NECROSIS) DOMAIN	➡	HEAT REPEAT
○	KELCH REPEAT	○	BP-BIPARTITE NUCLEAR LOCALIZATION SIGNAL	⊙	FOS/JUN DNA-BINDING DOMAIN	⊙	Zn-FINGER C ₂ H ₂
⊖	RING FINGER DOMAIN	⬭	TRANSFERASE DOMAIN	⬭	gi 1707204-DOMAIN	⬭	PROLINE-RICH REGION
⬭	FIBRONECTIN III DOMAIN	⬭	NEW A-DOMAIN	⬭	NEW HAT DOMAIN (HEMAGGLUTININ, ALPHA TOXIN, TUMOR NECROSIS-FACTOR-ALPHA-INDUCED PROTEIN)	⬭	PKC-C1 DOMAIN, CAG/PE-BINDING
⬭	CYCLIN REPEAT	⬭	NEW POZ-LINKER DOMAIN	⬭	DEATH DOMAIN	⬭	PKC-C2 DOMAIN
Δ	EGF-LIKE DOMAIN	⬭	NEW B-DOMAIN	⬭	KINASE DOMAIN	⬭	PROTEIN KINASE DOMAIN
⬭	CUB DOMAIN	⬭	NEW SPOD DOMAIN	⬭			
▲	LAMININ EGF-LIKE DOMAIN	⬭					

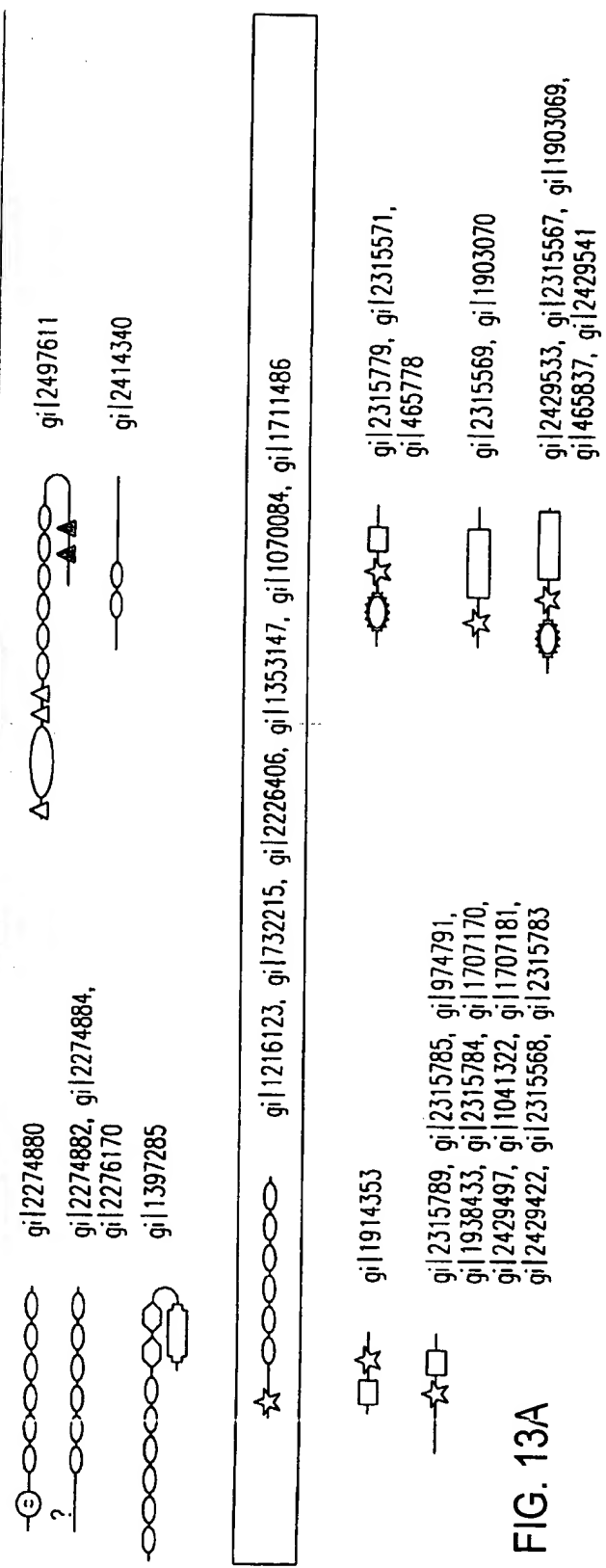
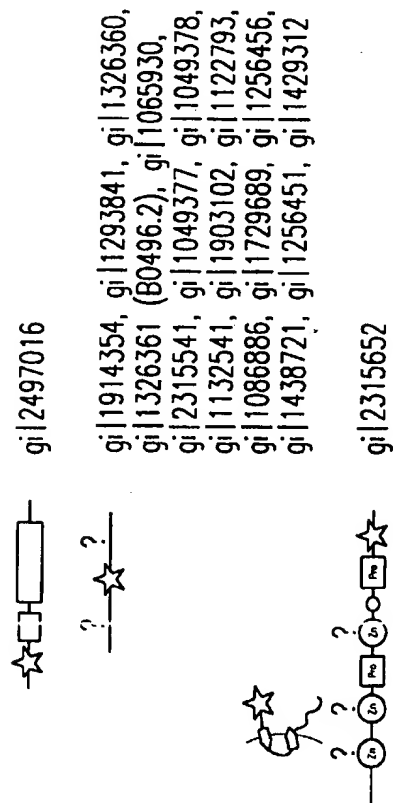
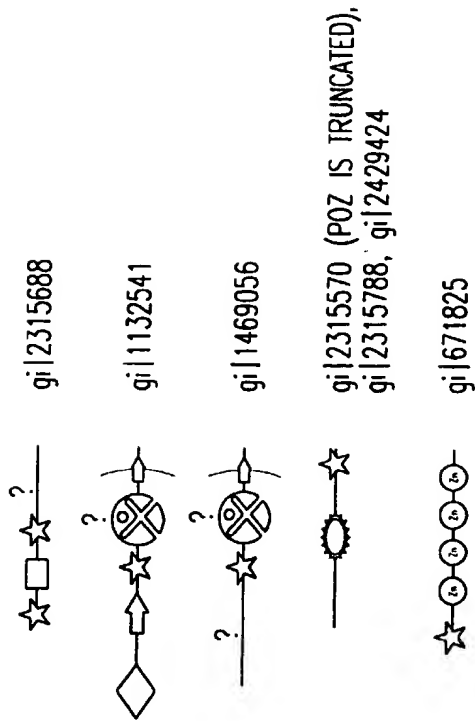


FIG. 13A





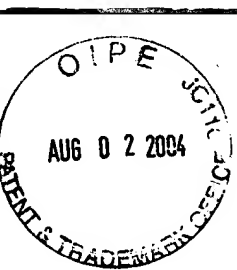


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>gi|2210766|gb|AA481214|AA481214 aa34e02.r1 NCI_CGAP_GCB1 Homo sapiens cDNA clone
IMAGE:815162 5' similar to WP:W07A12.4 CE03795 :, mRNA sequence [Homo sapiens]
CATGGCTTCCTGGACACCAACCCTGCCATCCGGGAGCAGACGGTCAAGTCCATGCTGCTCCTGGCCCCAA
AGCTGAACGAGGCCAACCTCAATGTGGAGCTGATGAAGCACCTTTGCACGGCTACAGGCCAAGGATGAACA
GGGCCCCATCCGCTGCAACACACAGTCTGCCCTGGGCAAAATGGGCTCCTACCTCAGTGTAGCACCAGA
CACAGGGTCTTACCTCTGCCTTCAGCGAGCCACTAGGGACCGGTTTGACCGTCCCGGGTTGCGGGTG
TCCTGGGCTTTGCTGCCACCCACAACCTCTACTCAATGAACGACTGTGCCCAAGATCCTGCCTGTGCT
CTGCGGTCTCACTGTAGATCCTGAGAAATCCGTGGAGACCAGGCCCTTCAAGGCA ID8

>gi|1349211|gb|W51957|W51957 zc45f01.r1 Soares_senescent_fibroblasts_NbHSF Homo
sapiens cDNA clone IMAGE:325273 5', mRNA sequence [Homo sapiens]
CCTTCGAGTTCGGCAATGCTGGGGCCGTTGTCTCACGCCCTCTTCAAGGTGGCAAGTTCTGAGCGC
TGAGGAGTATCAGCAGAAGATCATCCCTGTGGTGGTCAAGATGTTCTCATCCACTGACCGGGCCATGCCG
ATCCGNCTCCTGCAGCAGATGGAGCAGTTCATCCAGTACCTTGACGAGCCCAACAGTCAACACCCAGATCT
TCCCCACGTGTCATGGCTTCTGGACACCAACCCTGCCATCCGGGAGCAGACGGTCAAGTCCATGCT
GCTCCTGGCCCCAAAGCTGAACGAGGCCAACCTCAATGTGGAGCTGATGAAGCACTTTGCACGGCTACAG
GCCAAGGATGAACAGGGCCCCATCCGCTGCAACACCACAGTCTGCCCTGGGCAAAATCGGCTCCTACCTCA
GTGCTAGCACCAGACACAGGGTCTTACCTCTG ID9

FIG. 14A



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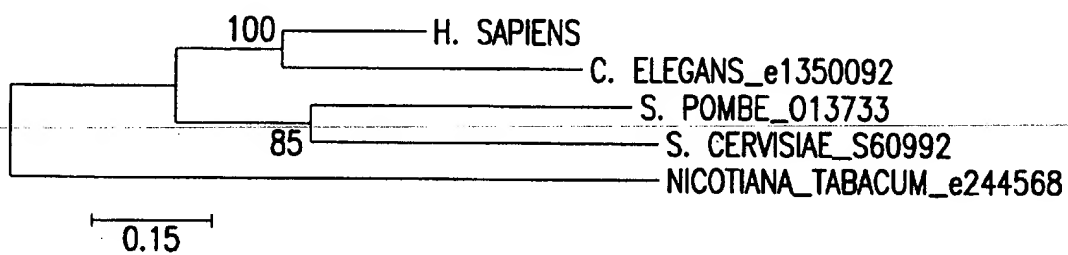


FIG. 14B



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BASE COUNT 405 a 545 c 493 g 278 t 6 others

ORIGIN

```
1  cagccgaagc amgcaaaaat tcttccagga gctgagcaag agcctggacg cattccctga
61  ggayttctgt cggcacaagg tgctgcccc a gctgctgacc gccttcgagt tcggcaatgc
121 tggggccggt gtcctcacgc ccctcttcaa ggtgggcaag ttcctgagcg ctgaggagta
181 tcagcagaag atcatccctg tgggtgtcaa gatgttctca tccactgacc gggccatgcg
241 catccgcctc ctgcagcaga tggagcagtt catccagtac cttgacgagc caacagtcaa
301 caccagatc ttccccacg tegtacatgg cttcctggac accaaccctg ccatccggga
361 gcagacggtc aagtccatgc tgctcctggc cccaaagctg aacgaggcca acctcaatgt
421 ggagctgatg aagcactttg cacggctaca ggccaaggat gaacagggcc ccatccgctg
481 caacaccaca gtctgcctgg gcaaaatcgg ctctacctc agtgctagca ccagacacag
541 ggtccttacc tctgccttca gccagaccac tagggaccgc tttgcaccgt cccgggttgc
601 ggggtgtcctg ggctttgctg ccaccacaa cctctactca atgaacgact gtgccagaa
661 gatcctgcct gtgctctgcg gtctcactgt agatcctgag aaatccgtgc gagaccaggc
721 cttcaaggcm wttcggagct tcctgtccaa attggagtct gtgtcggagg acccgacca
781 gctggaggaa gtggagaagg atgtccatgc agcctccagc cctggcatgg gaggagccgc
841 agctagctgg gcaggctggg cgtgaccggg gtctcctcac tcacctcaa gctgatccgt
901 tcgcaccaa cactgcccc aacagaaacc aacattcccc aaagaccac gcctgaagga
961 gttcctgccc cagccccac ccctgttctt gccacccta caacctcagg cactgggag
1021 acgaggagg aggacaagga cacagcagag gacagcagca ctgctgacag atgggacgac
1081 gaagactggg gcagcctgga gcaggaggcc gagtctgtgc tggcccagca ggacgactgg
1141 agcaccggg gccagttag ccgtgctagt caggtcagca actccgacca caaatcctcc
1201 aaatccccag agtccgactg gacagctgg gaartgagg gctcctggga acagggctgg
1261 caggagcaa gctcccagga gccacctyct gacggtacac ggctggccag cgagtataac
1321 tggggtggcc cagagtccag cgacaagggc gacccttcg ctacctgtc tgcacgtccc
1381 agcaccagc cgaggccaga ctcttggggt gaggacaact gggagggcct cgagactgac
1441 agtcgacagg tcaaggctga gctggcccgg aagaagcgcg aggagcggcg gcgggagatg
1501 gaggccaaac gcgccgagag gaaggtgcca agggcccat gaagctggga gcccggaagc
1561 tggactgaac cgtggcggtg gcccttccc gctgcggaga gcccggcca cagatgtatt
1621 tattgtacaa accatgtgag cccggccgcc cagccaggcc atctcacgtg tacataatca
1681 gagccacaat aaattctatt tcacaaaaa aaaaaaaaa aaaaaaa
```

//

FIG. 14C



	5	10	15	20	25	30																								
1	S	R	S	X	Q	K	F	F	Q	E	L	S	K	S	L	D	A	F	P	E	D	F	C	R	H	K	V	L	P	Q
31	L	L	T	A	F	E	F	G	N	A	G	A	V	V	L	T	P	L	F	K	V	G	K	F	L	S	A	E	E	Y
61	Q	Q	K	I	I	P	V	V	V	K	M	F	S	S	T	D	R	A	M	R	I	R	L	L	Q	Q	M	E	Q	F
91	I	Q	Y	L	D	E	P	T	V	N	T	Q	I	F	P	H	V	V	H	G	F	L	D	T	N	P	A	I	R	E
121	Q	T	V	K	S	M	L	L	L	A	P	K	L	N	E	A	N	L	N	V	E	L	M	K	H	F	A	R	L	Q
151	A	K	D	E	Q	G	P	I	R	C	N	T	T	V	C	L	G	K	I	G	S	Y	L	S	A	S	T	R	H	R
181	V	L	T	S	A	F	S	R	A	T	R	D	P	F	A	P	S	R	V	A	G	V	L	G	F	A	A	T	H	N
211	L	Y	S	M	N	D	C	A	Q	K	I	L	P	V	L	C	G	L	T	V	D	P	E	K	S	V	R	D	Q	A
241	F	K	A	X	R	S	F	L	S	K	L	E	S	V	S	E	D	P	T	Q	L	E	E	V	E	K	D	V	H	A
271	A	S	S	P	G	M	G	G	A	A	A	S	W	A	G	W	A													

ID11

FIG. 14D



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>sp|P15533|RPT1_MOUSE DOWN REGULATORY PROTEIN OF INTERLEUKIN 2 RECEPTOR
(J03776) rpt-1r [Mus musculus] Length = 353

Score = 92.0 bits (237), Expect = 6e-20

Query 194 VMELLEEDLTCPICCSLFDDPRVLPCSHNFCKKCLEGILEGSRNSMWRPAPFKCPTCRK 373
V+E+++E++TCPIC L +P C+H+FC+ C+ E S RN+ CP CR

Sbjct 5 VLEMIKEEVTCPICLELLKEPVSAHCNHSFCRACITLNYE-SNRNT---DGKGNCPCVRV 60

Query 374 ETSATGINSLQVNYSLKGIVEKYKIKISP----KMPVCKGHMGQPLNIFCLTDMQLICG 541
+L+ N + IVE+ K P K+ +C H G+ L +FC DM +IC

Sbjct-61 PYP---FGNLRPNLHVANIVERLKGFSIPEEEQKVNICAQH-GEKLRLFCRKDMMVICW-116

Query 542 ICATRGHTKHVFCSDI DAYAQERDAFESLFQSF-----ETWRRGDALSRLDTMETSK 700
+C EH H IE+ + ++ + + W+ L R+D

Sbjct 117 LCERSQEHGRHQTALIEEVDQEYKEKLQGALWKLKMKKAKICDEWQDDLQLQRVDW----- 171

Query 701 RKSLQLMTKDSKVKFEFFELQHTLDQKKNEILSDFETMKLAVMQAYDPEINKL 862
+Q+ + + V+ F+ L+ LD K+NE L + K VM+ + N+L

Sbjct 172 ENQIQI---NVENVQRQFKGLRDLLDSKENEELQKLKKEKKEVMEKLEESENEL 222

Homology covers ring finger, B-box and the beginning of coiled coil domain
in the CLL ring finger protein

FIG. 15



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ACTIVATED CD4⁺ T-CELLS

Rpt1 (REPRESSES EXPRESSION OF IL-2 RECEPTOR)

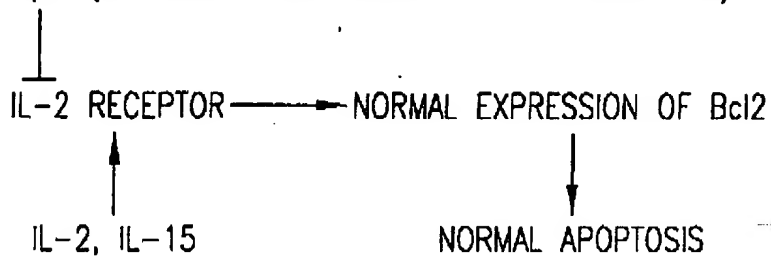


FIG. 16A

WHEN rpt1 IS KNOCKED OUT:

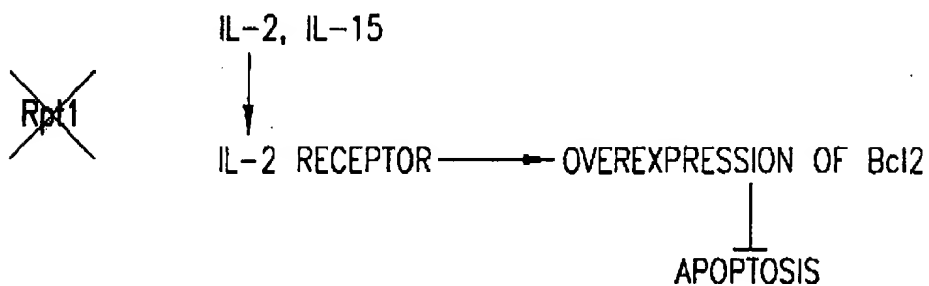


FIG. 16B



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TBLASTN 2.0.8 [Jan-05-1999]

Reference:

Altschul, Stephen F., Thomas L. Madden, Alejandro A. Schaffer,
Jinghui Zhang, Zheng Zhang, Webb Miller, and David L. Lipman (1997),
"Gapped BLAST and PSI-BLAST: a new generation of protein database search
programs", Nucleic Acids Res. 25.3389-3402.

Query= gi |2137498|Mad3m
(205 letters)

gb|AA278224|AA2278224 zs77e05.r1 NCI_CGAP_GCB1 Homo sapiens cDNA clone IMAGE:703520 5'
similar to TR:G1184157 G1184157 MAX-INTERACTING
TRANSCRIPTIONAL REPRESSOR. ;
Length = 430

Score = 209 bits (526), Expect = 1e-53
Identities = 104/124 (83%), Positives = 116/124 (92%), Gaps = 1/124 (0%)
Frame = +2

Query: 1	MEPVASNIQVLLQAAEFLERREREAEHGYASLCPHHSPGTVCRRRKPPLQAPGALNSGRS	60	ID14
	MEP+ASNIQVLLQAAEFLERREREAEHGYASLCPH SPG + RR+K P QAPGA +SGRS		ID15
Sbjct: 56	MEPLASNIQVLLQAAEFLERREREAEHGYASLCPHRSPGPIHRRKKRPPQAPGAQDSGRS	235	ID16

Query: 61	VHNELEKRRRAQLKRCLEQLRQQMPLGVDCTRYTTLSELL-RARVHIQKLEEQEQQARRLK	119	
	VHNELEKRRRAQLKRCLE+L+QQMPLG DC RYTTLSELL RAR+HIQKLE+QEQ+AR+LK		
Sbjct: 236	VHNELEKRRRAQLKRCLERLKQQMPLGGDCARYTTLSELLRRARMHIQKLEDQEQRARQLK	415	

Query: 120	EKLRS 124		
	E+LR+		
Sbjct: 416	ERLRT 430		

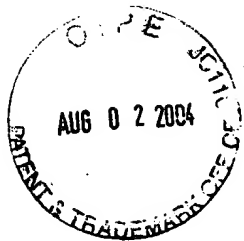
dbj|C02407|C02407 HUMGS0012279, Human Gene Signature, 3'-directed cDNA sequence.
Length = 348

Score = 97.5 bits (239), Expect = 6e-20
Identities = 51/63 (80%), Positives = 56/63 (87%)
Frame = +3

Query: 125	KQQSLQQLEQLQGLPGARERERLRADSLDSSGLSSERSDSQEDLEVDVENLVFGTETE	184	ID17
	KQQSLQ+ QL+GL GA ERERLRADSLDSSGLSSERSDSQE+LEVDVE+LVFG E E		ID18
Sbjct: 45	KQQSLQRXWMQLRGLAGAAERERLRADSLDSSGLSSERSDSQEELEVDVESLVFGGEAE	224	ID19

Query: 185	LLQ 187		
	LL+		
Sbjct: 225	LLR 233		

FIG. 17A



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BASE COUNT 130 a 234 c 258 g 106 t 5 others
ORIGIN

```
1  cagccgcttg ctccggccgg caccctaggc cgcagtcgcg caggctgtcg ccgacatgga
61 acccttggcc agcaacatcc aggtcctgct gcaggcggcc gagttcctgg agcgccgtga
121 gagagaggcc gagcatggtt atgcgtccct gtgcccgcat cgcagtcag gccccatcca
181 caggaggaag aagcgacccc cccaggctcc tggcgcgag gacagcgggc ggtcagtga
241 caatgaactg gagaagcgca ggagggccca gttgaagcgg tgcctggagc ggctgaagca
301 gcagatgccc ctgggcggcg actgtgcccg gtacaccacg ctgagcctgc tgcgccgtgc
361 caggatgcac atccagaagc tggaggatca ggagcagcgg gcccgacagc tcaaggagag
421 gctgcgcaca aagcagcaga gcctgcagcg gcantggatg cagctccggg ggctggcagg
481 ngcgcccgag cgggagcgnc tgcgggcgga cagtctggac tcctcaggcc tctcctctga
541 gcgctcagac tcagaccaag aggagctgga ggtggatgtg gagagcctgg tgtttggggg
601 tgaggccgag ctgctgcggg gcttcgtcgc cgccaggag cacagctact cgcacgtcgg
661 cggcgcttg ctatgatgtt cctcaccan ggcgggcctc tgccctctta ctcgttgccc
721 aagcccactt tnc
```

FIG.17B



>Mad3b(Putative)
MEPLASNIQVLLQAAEFLERREREAEHGYASLCPHRSPGPIHRRKKRPPQAPGAQDSGRSVHNELEKRRRAQLK
RCLERLXQQMP LGDCARYTTLSLLRRARHITQKLEDEQRARQLKERLTKQSLQRXWMLRGLAGAAERER
LRADSLDSSGLSSERSDSDOEELEVDVESLVFGGEALLRGFVAGOEHSYSHVGGAWL ID27

FIG. 17C

gi 2506888 MADe	MATAVGHNIIQLLLEAADYLERREREAEHGYASMLPYS-KDADFRRINKPKKNST--SSRSTHNEKRRRAHLRLCLEKGLVPLGPSSRHTTLSLL	ID21
gi 729978 MA3h	MAAYRMNIQMLLEAADYLERREREAEHGYASMLPYNKORDALKRRINKSKNNS--SSRSTHNEKRRRAHLRLCLEKLLGLVPLGPSSRHTTLSLL	22
gi 2792362 Mad4h	---MEINSLIILEAAEYLERROREAEHGYASVLPFDGDFAREKTKAAGLVRKAP--NNRSSHNELEKHRRAKRLYLEQLKQLVPLGPDSTRHTTLSLL	23
gi 2137499 Mad4m	---MEINSLIILEAAEYLERROREAEHGYASMLPFDGDFAREKTKTAGLVRKGP--NNRSSHNELEKHRRAKRLYLEQLKQLGPLGPDSTRHTTLSLL	24
gi 2137498 Mad3m	-MEPVASNIQVLLQAAEFLERREREAEHGYASLCPHSPGTVCRRRKPPQLAPGALNSGRSVHNELEKRRRAQLKRCLEQLRQQMP LGVDCTRYTTLSLL	25
Mad3h Putative	-MEPLASNIQVLLQAAEFLERREREAEHGYASLCPHRSPGPIHRRKKRPPQAPGAQDSGRSVHNELEKRRRAQLKRCLEQLRQQMP LGGDCARYTTLSLL	26

gi 2506888 MADe	TKAKLHIKKLEDCORKAVHQIDQLQREQRHLLKRRLEKGAERTR-----MDSVG-SVYSSERSDSRELDVDVDVDVDVEGTDYLPGLQWSSS-	
gi 729978 MA3h	TKAKLHIKKLEDCORKAVHQIDQLQREQRHLLKRRLEKLGIERIR-----MDSIG-STVSSERSDSRE-----EIDVDVESTDYLTGDLDMSSSS	
gi 2792362 Mad4h	KRAKVHIKKLEEQRRALSIKEQLQEQHFLKRRLEQLSVQSVR-----VRTDTG-SAVSTD--DSEQE-----VDIEGMEFGPGELDSVGS-	
gi 2137499 Mad4m	K-AKVHIKKLEEQRRALSIKEQLQEQHFLKRRLEQLSVQSVR-----VRTDTG-SAVSTD--DSEQE-----VDIEGMEFGPGELDSVGS-	
gi 2137498 Mad3m	R-ARVHIQKLEEQEQARRLKEKLPKSKQSLQQQLQGLPGARERPLRADSLDSSGLSSERSDSQD-----DLSVDVENLVFG-TETELLQSF	
Mad3h Putative	RRARMHIQKLEDEQQRARQLKERLRTKQSLQRXWMLRGLAGAAERERLRADSLDSSGLSSERSDSQD-----ELEVDESIVFG-GEALLRGF	

gi 2506888 MADe	VSDSDESGSMQSLG-SDEGYSSATYKRAKLQQGHKAGLGL	
gi 729978 MA3h	VSDSDESGSMQSLG-SDEGYSSSTSIKRIKLQSHKACLGL	
gi 2792362 Mad4h	SSDADHDHYSLSQSGTGSDGSGFGPHCRRLGRPAL-----	
gi 2137499 Mad4m	SSDADHDHYSLSQSGSDSSYGHPCRRPGCPGLS-----	
gi 2137498 Mad3m	SAGREHSYSHSTCAWL-----	
Mad3h Putative	VAGQEHSHVGGAWL-----	

FIG. 17D

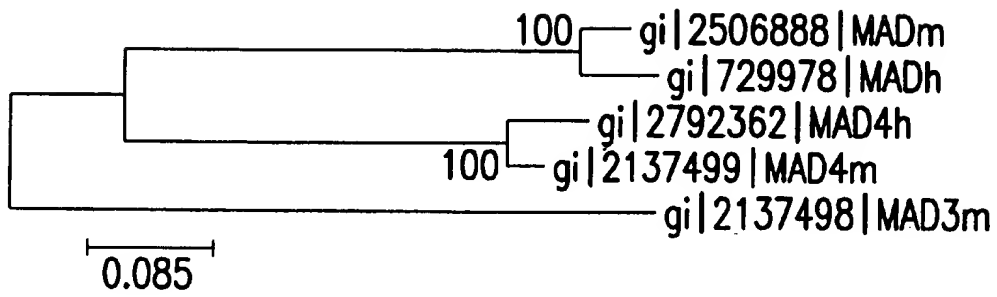


FIG. 18A

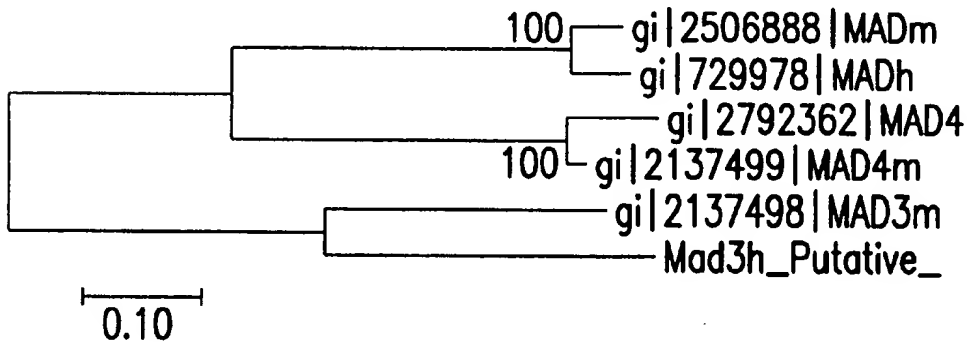


FIG. 18B